

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. to 7. (Cancelled).
8. (Withdrawn) A method of treating neurodegeneration in a patient, comprising
  - identifying a patient at risk for neurodegeneration; and
  - administering to the patient a therapeutically effective amount of a Ubiquitination activator.
9. (Withdrawn) The method of claim 8, wherein the Ubiquitination activator is an activator of E1 Ubiquitin activating enzyme.
10. (Withdrawn) The method of claim 8, wherein the Ubiquitination activator is an activator of E1 Ubiquitin conjugating enzyme.
11. (Withdrawn) The method of claim 8, wherein the Ubiquitination activator is an activator of E3 Ubiquitin ligating enzyme.
12. (Withdrawn) A method of treating neurodegeneration in a patient, comprising
  - identifying a patient at risk for neurodegeneration; and
  - administering to the patient a therapeutically effective amount of deUbiquitination inhibitor.

**Appln No. 10/789,518**  
**Reply to Office action of July 28, 2006**

13. (Withdrawn) The method of claim 12, wherein the deUbiquitination inhibitor is an inhibitor of Ubiquitin isopeptidase.

14. (Withdrawn) A method of treating polyglutamine-expansion-related neurodegeneration in a patient, comprising  
identifying a patient at risk for polyglutamine-expansion-related neurodegeneration; and  
administering to the patient a therapeutically effective amount of SUMOylation blocker.

15. (Withdrawn) The method of claim 14, wherein the SUMOylation blocker is an inhibitor E1 SUMO activating enzyme.

16. (Withdrawn) The method of claim 14, wherein the SUMOylation blocker is an inhibitor E2 SUMO conjugating enzyme.

17. (Withdrawn) The method of claim 14, wherein the SUMOylation blocker is an inhibitor E3 SUMO ligating enzyme.

18. (Withdrawn) The method of claim 17, wherein the inhibitor of E3 SUMO ligating enzyme is a PIAS protein.

19. (Withdrawn) A method of treating polyglutamine-expansion-related neurodegeneration in a patient, comprising  
identifying a patient at risk for polyglutamine-expansion-related neurodegeneration; and  
administering to the patient a therapeutically effective amount of deSUMOylation enhancer.

**Appln No. 10/789,518**  
**Reply to Office action of July 28, 2006**

20. (Withdrawn) The method of claim 19, wherein the deSUMOylation enhancer is SUMO isopeptidase.

21. (Withdrawn) A method of treating polyglutamine-expansion-related neurodegeneration in a patient, comprising  
identifying a patient at risk for polyglutamine-expansion-related neurodegeneration; and  
administering to the patient a therapeutically effective amount of a Ubiquitination activator.

22. (Withdrawn) The method of claim 21, wherein the Ubiquitination activator is an activator of E1 Ubiquitin activating enzyme.

23. (Withdrawn) The method of claim 21, wherein the Ubiquitination activator is an activator of E2 Ubiquitin conjugating enzyme.

24. (Withdrawn) The method of claim 21, wherein the Ubiquitination activator is an activator of E3 Ubiquitin ligating enzyme.

25. (Withdrawn) A method of treating polyglutamine-expansion-related neurodegeneration in a patient, comprising  
identifying a patient at risk for polyglutamine-expansion-related neurodegeneration; and  
administering to the patient a therapeutically effective amount of deUbiquitination inhibitor.

26. (Withdrawn) The method of claim 25, wherein the deUbiquitination inhibitor is an inhibitor of Ubiquitin isopeptidase.

**Appln No. 10/789,518**  
**Reply to Office action of July 28, 2006**

27. (Withdrawn) A method of treating a neurodegenerative disease in a patient, comprising administering to the patient a therapeutically effective amount of SUMOylation blocker.

28. (Withdrawn) The method of claim 27, wherein the SUMOylation blocker is an inhibitor E1 SUMO activating enzyme.

29. (Withdrawn) The method of claim 27, wherein the SUMOylation blocker is an inhibitor E2 SUMO conjugating enzyme.

30. (Withdrawn) The method of claim 27, wherein the SUMOylation blocker is an inhibitor E3 SUMO ligating enzyme.

31. (Withdrawn) The method of claim 30, wherein the inhibitor of E3 SUMO ligating enzyme is a PIAS protein.

32. (Withdrawn) The method of claim 27, wherein the neurodegenerative disease is one of more of the group consisting of Huntington's disease, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Kennedy's disease, SCA1, DRPLA, epilepsy, diabetes mellitus, spongiform encephalopathy, prion-related disease, Machado-Joseph's disease and schizophrenia.

33. (Withdrawn) A method of treating a neurodegenerative disease in a patient, comprising administering to the patient a therapeutically effective amount of deSUMOylation enhancer.

34. (Withdrawn) The method of claim 33, wherein the deSUMOylation enhancer is SUMO isopeptidase.

**Appln No. 10/789,518**  
**Reply to Office action of July 28, 2006**

35. (Withdrawn) The method of claim 33, wherein the neurodegenerative disease is one of more of the group consisting of Huntington's disease, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Kennedy's disease, SCA1, DRPLA, epilepsy, diabetes mellitus, spongiform encephalopathy, prion-related disease, Machado-Joseph's disease and schizophrenia.

36. (Withdrawn) A method of treating a neurodegenerative disease in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

37. (Withdrawn) The method of claim 36, wherein the Ubiquitination activator is an activator of E1 Ubiquitin activating enzyme.

38. (Withdrawn) The method of claim 36, wherein the Ubiquitination activator is an activator of E1 Ubiquitin conjugating enzyme.

39. (Withdrawn) The method of claim 36, wherein the Ubiquitination activator is an activator of E3 Ubiquitin ligating enzyme.

40. (Withdrawn) A method of treating a neurodegenerative disease in a patient, comprising administering to the patient a therapeutically effective amount of a deUbiquitination inhibitor.

41. (Withdrawn) The method of claim 40, wherein the deUbiquitination inhibitor is an inhibitor of Ubiquitin isopeptidase.

42. (Withdrawn) The method of claim 40, wherein the neurodegenerative disease is one of more of the group consisting of Huntington's disease, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Kennedy's disease, SCA1,

**Appln No. 10/789,518**  
**Reply to Office action of July 28, 2006**

DRPLA, epilepsy, diabetes mellitus, spongiform encephalopathy, prion-related disease, Machado-Joseph's disease and schizophrenia.

43. (Withdrawn) A method of treating Huntington's disease in a patient, comprising administering to the patient a therapeutically effective amount of a SUMOylation blocker.

44. (Withdrawn) A method of treating Huntington's disease in a patient, comprising administering to the patient a therapeutically effective amount of a deSUMOylation enhancer.

45. (Withdrawn) A method of treating Huntington's disease in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

46. (Withdrawn) A method of treating Huntington's disease in a patient, comprising administering to the patient a therapeutically effective amount of a deUbiquitination inhibitor.

47. (Withdrawn) A method of treating Kennedy's disease in a patient, comprising administering to the patient a therapeutically effective amount of a SUMOylation blocker.

48. (Withdrawn) A method of treating Kennedy's disease in a patient, comprising administering to the patient a therapeutically effective amount of a deSUMOylation enhancer.

**Appln No. 10/789,518**  
**Reply to Office action of July 28, 2006**

49. (Withdrawn) A method of treating Kennedy's disease in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

50. (Withdrawn) A method of treating Kennedy's disease in a patient, comprising administering to the patient a therapeutically effective amount of a deUbiquitination inhibitor.

51. (Withdrawn) A method of treating spinocerebellar ataxia in a patient, comprising administering to the patient a therapeutically effective amount of a SUMOylation blocker.

52. (Withdrawn) A method of treating spinocerebellar ataxia in a patient, comprising administering to the patient a therapeutically effective amount of a deSUMOylation enhancer.

53. (Withdrawn) A method of treating spinocerebellar ataxia in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

54. (Withdrawn) A method of treating spinocerebellar ataxia in a patient, comprising administering to the patient a therapeutically effective amount of a deUbiquitination inhibitor.

55. (Withdrawn) A method of treating dentatorubral-pallidoluysian atrophy in a patient, comprising administering to the patient a therapeutically effective amount of a SUMOylation blocker.

**Appln No. 10/789,518**  
**Reply to Office action of July 28, 2006**

56. (Withdrawn) A method of treating dentatorubral-pallidoluysian atrophy in a patient, comprising administering to the patient a therapeutically effective amount of a deSUMOylation enhancer.

57. (Withdrawn) A method of treating dentatorubral-pallidoluysian atrophy in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

58. (Withdrawn) A method of treating dentatorubral-pallidoluysian atrophy in a patient, comprising administering to the patient a therapeutically effective amount of a deUbiquitination inhibitor.

59. (Withdrawn) A method of treating protein-aggregation-related neurodegeneration in a patient, comprising administering to the patient a therapeutically effective amount of a SUMOylation blocker.

60. (Withdrawn) A method of treating protein-aggregation-related neurodegeneration in a patient, comprising administering to the patient a therapeutically effective amount of a deSUMOylation enhancer.

61. (Withdrawn) A method of treating protein-aggregation-related neurodegeneration in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

62. (Withdrawn) A method of treating protein-aggregation-related neurodegeneration in a patient, comprising administering to the patient a therapeutically effective amount of a deUbiquitination inhibitor.



**Appln No. 10/789,518**  
**Reply to Office action of July 28, 2006**

63. (Withdrawn) A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a SUMOylation blocker.

64. (Withdrawn) A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a deSUMOylation enhancer.

65. (Withdrawn) A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a Ubiquitination activator.

66. (Withdrawn) A method of treating Machado-Joseph's disease in a patient, comprising administering to the patient a therapeutically effective amount of a deUbiquitination inhibitor.

67. (New) A method of treating neurodegeneration in a patient, comprising identifying a patient diagnosed with neurodegeneration; and administering to the patient a therapeutically effective amount of an agent for reducing protein SUMOylation.

68. (New) The method of claim 67, wherein the agent is a SUMOylation blocker.

69. (New) The method of claim 68, wherein the SUMOylation blocker is an inhibitor of E1 SUMO activating enzyme.

70. (New) The method of claim 68, wherein the SUMOylation blocker is an inhibitor of E2 SUMO conjugating enzyme.

71. (New) The method of claim 68, wherein the SUMOylation blocker is an inhibitor of E3 SUMO ligating enzyme.

72. (New) The method of claim 71, wherein the E3 SUMO ligating enzyme is a PIAS protein.

73. (New) The method of claim 67, wherein the agent is a deSUMOylation enhancer.

74. (New) The method of claim 73, wherein the deSUMOylation enhancer enhances SUMO isopeptidase activity.

75. (New) The method of claim 67 wherein the neurodegenerative disease is polyglutamine-expansion-related neurodegeneration.

76. (New) The method of claim 67 wherein the neurodegenerative disease is protein-aggregation-related neurodegeneration.

77. (New) The method of claim 67 wherein the neurodegenerative disease is one of more of the group consisting of Huntington's disease, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Kennedy's disease, SCA1, DRPLA, epilepsy, diabetes mellitus, spongiform encephalopathy, prion-related disease, Machado-Joseph's disease and schizophrenia.